

***Remarks***

Upon entry of the foregoing amendment, claims 1-25 are pending in the application, with claims 1 and 18 being the independent claims. Support for new claims 22-25 can be found, *inter alia*, in claim 16, at pages 6-7, paragraph 23, at page 9, paragraph 33 through page 11, paragraph 36, and at page 11, paragraph 38, of the application as filed.

This amendment is believed to introduce no new subject matter and its entry is respectfully requested.

***Rejection under 35 U.S.C. § 103 (claims 1-21)***

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kempe (U.S. Patent No. 5,514,789) in view of Lytle *et al.* (*Nucleos. Nucleot.*, 18:1809-1824 (1999)). Applicants respectfully traverse this rejection.

Specifically, the Examiner is of the opinion that:

It would have been obvious to one of ordinary skill in the art to employ the cleavage protocol using the gaseous nucleophile ammonia as taught by Kempe *et al.* with the vicinal heteroatom containing linkers as taught by Lytle *et al.* One of ordinary skill in the art would have been motivated to do so because Lytle *et al.* teach that the use of such universal linkers expedites oligo synthesis by facilitating easier use of multiple well plates (Intro., line 6), and since Kempe *et al.* teach that use of a gaseous nucleophilic ammonia enhances efficacy by significantly reducing the time required for recovery of synthesized oligonucleotides.

(OGE) Action, pages 3, lines 15-21). Applicants respectfully disagree with the Examiner's

Kempe is directed to a method of cleaving synthesized oligonucleotides from solid supports using a gaseous ammonia reagent. Kempe does not teach the cleavage of a universal linker from an oligonucleotide and solid support. Lyttle *et al.* teach a universal linker, which remains bound to the solid support after cleavage from the oligonucleotide. In fact, Lyttle *et al.* teach away from the use of universal linkers, as a means to facilitate automated oligonucleotide synthesis, when strongly basic reagents are used in the oligonucleotide cleavage reaction.

It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983).

Lyttle *et al.* teach that:

Post synthesis cleavage protocols involve either strongly basic conditions with heating at elevated temperatures for long periods, or the use of alkali metal salts which require additional steps for removal. These limitations have, so far, outweighed the added convenience of one support material for every sequence, and *prederivatized supports are still predominantly preferred.*

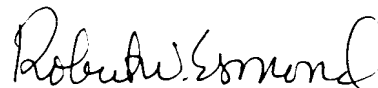
(Page 1809, lns. 10-14, emphasis added, citation omitted). Thus, Lyttle *et al.* teach that strongly basic conditions are a limitation. Because Kempe teaches the use of gaseous ammonia (i.e. strongly basic conditions) for cleavage, one of ordinary skill in the art would not have modified the standard linker in Kempe. One of ordinary skill in the art would not have believed that such modification would offer any benefit to automated oligonucleotide synthesis. Therefore, there would have been no motivation to combine the teachings of Kempe and Lyttle, *et al.* Applicants respectfully submit that the rejection of claims 1-21 is

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

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1100 New York Avenue, N.W.  
Suite 600  
Washington, D.C. 20005-3934  
(202) 371-2600

**Version with markings to show changes made**

***In the Claims:***

Claims 22-25 were added.